

REMARKS

An appeal was made in the parent case. In its decision, the Board affirmed that Examiner made a *prima facie* case of obviousness against claims that were narrower in scope than those claims filed herein. The Board also alleged that the data presented in the specification fails to show unexpected results in terms of efficacy of the claimed combination therapy.

Further the Board alleged that “it is impossible to conclude from Table II (in the specification) that the incidence of adverse events was consistently lower in patients treated with mid- or high-potency corticosteroid in combination with tazarotene as compared with patients treated with low potency-corticosteroid in combination with tazarotene, or tazarotene alone.” Applicant responds with arguments and further support in the form of data in a scientific publication, that the claimed combination does in fact have unexpected benefits over the use of tazarotene alone in terms of adverse events. The trend in the total number of adverse events points to a significant advantage for the tazarotene/corticosteroid combination.

Consider that the table below, which gives the total number of adverse events for each treatment taken from Table II, clearly shows that the frequency of adverse events decreases as the corticosteroid potency increases in the combination therapy.

| | Patients (%) | | | |
|----------------------|--------------|---------|---------|----------|
| | Taz/plac | Taz/low | Taz/med | Taz/high |
| Total Adverse Events | 41 | 39 | 31 | 26 |

For additional support of this position, Applicant submits herewith a reference by Gollnick (*British Journal of Dermatology* 1999; 140 (Suppl. 54): 18-23), published after the effective filing date of the present application, which is therefore not prior art, which supports Applicant’s assertion that corticosteroids in combination with tazarotene have fewer side effects. The reference states “there was a trend towards a lower incidence of treatment-related adverse events as corticosteroid potency increased (from 42% with tazarotene plus placebo to 36%, 32%, and 31% with tazarotene plus the low-, mid-, and high potency corticosteroid, respectively).” The combination of the results presented in the present application and the teachings of the cited reference provide sufficient support for our conclusion that the presently claimed

compositions have fewer side effects. A person of ordinary skill in the art would expect that when two therapies are combined, the number of adverse events would be greater compared to the individual monotherapies, i.e. the adverse events would be additive. As shown in the specification and the Gollnik reference, the use of a corticosteroid actually reduces the adverse events associated with the use of tazarotene. In a sense, the corticosteroid could be viewed as an agent that is effective in counteracting part of the adverse effects of tazarotene. The Gollnik reference states (p. 22, under Discussion) “[t]he corticosteroid enhances efficacy and ameliorates the perilesional irritation that may arise with topical retinoids such as tazarotene”. In summary, since the combination therapy is shown herein to reduce the number of adverse events associated with tazarotene, Applicant has demonstrated that the combination has unexpected properties, and is thus not obvious in view of the prior art.

In light of the points raised above, Applicant believes that the claims are patentable as they stand, and respectfully requests that Examiner pass them to issue.

Respectfully submitted,

Brent A. Johnson
Brent A. Johnson
Registration No. 51,851
Agent of Record

Please send all inquiries and correspondence to:

Brent A. Johnson
Allergan, Inc.
2525 Dupont Drive
Irvine, CA 92612
Telephone: 714/246-4348
Telecopier: 714/246-4249

CERTIFICATE OF EXPRESS MAIL UNDER 37 C.F.R. §1.10

I hereby certify that this Preliminary Amendment and the documents referred to as enclosed herein are being deposited with the United States Postal Service on April 7, 2004 in an envelope as "Express Mail Post Office To Addressee" mailing label number EV193721147US with sufficient postage for Express Mail addressed to Mail Stop: Patent Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Susan Bartholomew

Name of person mailing paper

Susan Bartholomew

Signature of person mailing paper

Date: April 7, 2004